Our Thanks to Neutrogena

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We salute Neutrogena for their contribution to the Endowment Fund and for their continued support of clinical and investigative dermatology.

D.A.N., Denver, CO.

In This Issue . . .

Jean L. Marx

Light Causes the Isomerization of Retin-A Applied to the Skin

Retin-A has been a widely used drug, first for treating acne and more recently for combating the wrinkles caused by sun exposure. Somewhat surprisingly then, researchers who have been investigating the actions of Retin-A, which also goes by the name tretinoin, have generally failed to consider that it might be converted in the skin to other products, some of which might contribute to the drug's therapeutic effects. "Scientists have a tendency to attribute the effects of tretinoin to tretinoin," says Paul Lehman of the National Center for Toxicologic Research in Jefferson, Arkansas. "But I've always questioned that. Retinoids are very sensitive to light."

In this issue, Lehman and Andrew Malany of the University of Washington in Seattle report that light converts tretinoin that has been applied to the skin to isotretinoin plus several additional, but as yet unidentified, retinoids. They determined this by first applying a commercial cream containing tretinoin to samples of cadaver skin and then exposing the samples to fluorescent light similar to that found in an ordinary office environment. When the researchers analyzed the retinoids in the skin samples 24 hours later, they found that 25% of the original tretinoin remained as tretinoin. Another 38% had been isomerized to isotretinoin, and the remaining 37% had been converted to a complex of retinoids that the researchers have not yet identified.

The finding suggests, Lehman says, that some of the effects attributed to tretinoin may instead be produced by isotretinoin, which has also been shown to be active in combating acne and wrinkles. In addition, the work raises concerns that some of the unidentified compounds produced by tretinoin might have untoward effects. "We don't know what they are or what they are doing. They could be harmful — or not," Lehman says.

The concern is heightened by the possibility that people who are trying to avoid wrinkles will use Retin-A for extended time periods — years, or even decades. The only experience with the drug until now has been for treating acne, which requires that it be used only for months at a time. "Historically it's very safe for short periods of time, but we don't know what will happen if you use it for years," Lehman remarks. The next step then is to find out just what the unidentified retinoids might be and what activity, if any, they might have in the skin.

Lehman also points out that the type of light hitting the skin influences the spectrum of compounds to which Retin-A will be converted. Previous studies of the drug's activity did not take into account the possibility that light might influence the retinoid content of the skin and possibly the study outcome. The researcher recommends that in future experiments light exposures should be controlled whenever possible.

Two Groups Make Progress Toward Understanding Melanin Synthesis

Despite the importance of melanin in determining skin coloration and protecting against the damage caused by exposure to ultraviolet light, the basic biologic mechanisms controlling the synthesis of the pigment are poorly understood. Two papers in this issue may help remedy this situation, however. In one, Philip Gordon and Barbara Gilchrest of Tufts University in Boston report surprising new information about the intracellular signalling pathway that tells human melanocytes to make melanin. In the other, researchers from the medical schools at Indiana University and Yale University describe research that should help provide a better understanding of how the gene for a key enzyme in the melanin synthetic pathway is controlled.

Most research on the control of melanin synthesis has been done on mouse melanoma cells, primarily because they grow readily in culture, whereas researchers have had trouble culturing normal human melanocytes. Recently, however, Gordon and Gilchrest devised an effective culture system for human melanocytes. While exploring melanogenesis in these cells they made an unexpected observation.

When melanocytes are exposed to ultraviolet radiation they re-

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